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IN ENTERIC FEVER.¹

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APPEARANCES IN ONE CASE.

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AMONG the rarer complications of enteric fever is that of pyelitis, though it is one which is well recognised as having an etiological relationship with that disease. The diagnosis has, however, points of difficulty, as in cases of enteric pyelitis some degree of nephritis is also present, especially at the onset, and while clinically I have been accustomed to regard this nephritis as due to a focal lesion in the kidney, which probably originates at the same time as the pyelitis, I have had up to the present moment no opportunity of verifying this inference by a *post-mortem* examination.

The cases number five in all, and the following is a brief record of their clinical course:—

CASE I.—P. Q., male, æt. 15. This patient suffered from a mild attack of enteric fever, the temperature falling to normal about the twenty-second day of illness. Had not the right ventricle become markedly dilated towards the end of the attack, and severe abdominal pain been present at intervals, there would have been nothing special about the course of the case. Towards the end of the fourth week from the commencement of the illness, however, a very severe relapse began, marked by a degree of prostration and cardiac weakness much in excess of that observed in the initial illness.

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Until nearly the end of this relapse the only sign of renal affection was the occasional presence of a trace of albumen in the urine. On the forty-third day of illness when the temperature had fallen almost to normal and the patient was much better, the urine passed at night was found to contain a considerable quantity of blood, and on the sediment being examined many blood corpuscles, some pyriform epithelial cells, and a few pus cells were found. During the next two days the urine was very deeply coloured with blood pigment, though the reaction to the guaiacum test was much less than the colour of the urine would have warranted on expectation. On the third day a large quantity of albumen was present, and many epithelial and granular tube-casts and pus cells were observed amid a great abundance of altered red blood corpuscles. From this point the amount of blood in the urine rapidly diminished, till in seven days from the first appearance it had completely vanished, though the last two or three days its presence was demonstrated microscopically as the guaiacum test failed to give a reaction. The amount of albumen decreased at the same time, and in a few days the sediment in the urine consisted of pus cells alone, to which the amount of albumen no more than corresponded. From the fifth day of the special illness onwards no tube-casts were observed, and from this time the amount of pus gradually diminished. On the twentieth and twenty-first days from the onset of symptoms there was no pus in the urine. On the twenty-second the left kidney could be quite easily palpated. A specimen of the urine passed some hours after contained a very large quantity of pus with a trace of blood, and in the evening when the abdomen was re-examined nothing could be made out in the region of the left kidney. From this point onwards, convalescence was uninterrupted, though when the patient was dismissed two months later a trace of pus was still present in the urine.

CASE II.—W. S., male, æt. 35. This case was very similar to the preceding, though the renal symptoms supervened towards the end of a primary fever and not of a relapse. The onset was associated with some degree of nephritis, much albumen being present in the urine and numerous tube-casts, as well as blood and catarrhal epithelial cells. By the third day much pus was present, epithelial and granular tube-casts were observed for five or six days, and after these had disappeared pus, associated occasionally with blood, continued to be present for more than three weeks, and when the

patient was dismissed two months later the former was still present in very small quantity. Albumen was abundant in the urine during the initial nephritis, and thereafter only in proportion to the amount of pus present in the urine, except on one occasion for a few days when it was more abundant than the pus warranted, but careful search at this period revealed no tube-casts.

CASE III.—D. D., male, æt. 36. This patient passed through a moderately severe attack of enteric fever, complicated with true lobar pneumonia and pleurisy. The case ended by lysis during the fourth week. A few days after the temperature was normal, a specimen of the urine passed in the evening was found deeply coloured with blood. As in the previous cases the guaiacum reaction was much less than might have been expected. Albumen was present, but probably not in any greater quantity than that accounted for by the amount of blood. The sediment on examination consisted chiefly of altered red blood corpuscles, with some small amount of dark-looking pigment granules, and epithelial cells, but no tube-casts. The succeeding specimens of urine passed were much clearer, and next day the blood had disappeared. For a few days thereafter a mere trace of albumen was present, and in the mucin deposit, which collected in the base of the urine-glass, it was noted that pus cells were present. In six days from the onset of symptoms the urine was clear, convalescence was very good, and the patient was dismissed well.

CASE IV.—W. M., female, æt. 11. This patient suffered from a typical attack of enteric fever, the temperature falling to normal on the twenty-fourth day. On the twenty-eighth day of illness, when the temperature was normal, she complained of pain on micturition, and the urine was found to be of a bright red tint, and there was a deposit of pus. During the next four days the pigment was absent, and the guaiacum reaction was not obtained, though pus still continued present. On the twenty-third day of illness I first saw this patient (she was then on the third day of a relapse), the urine was coloured with blood, the sediment contained many altered red blood cells, many pus cells, mixed with small shreddy bright red masses. On the thirty-sixth day of the fever blood was absent from the urine. The region of the left kidney was on this day tender to bimanual palpation. From this time the patient ran the course of an ordinary relapse, lasting till the forty-first day of illness, and had varying

amounts of pus in her urine, but only blood on one occasion. The amount of pus gradually diminished, and it was completely absent on the fifty-second day of illness. Albuminuria was present throughout, but not out of proportion to the amount of blood and pus. Convalescence was very good.

CASE V.—N. L., male, æt. 22. This patient was of Italian nationality, and, according to the history, sickened only eight days prior to admission. From the fact, however, that certain portions of the Peyer's patches in the ileum near to the ileo-cæcal valve were found *post-mortem* to lack foveation and to have a smooth surface, a condition found in healed enteric ulcers, it is probable that the patient was admitted during a severe relapse following an ambulatory attack of the disease. On admission the patient was very ill, and though the pulse was not very rapid it was of very poor quality. Tympanitis and a certain amount of rigidity of the abdomen were present. The spleen was much enlarged, and rose spots were noted. Although the temperature began to subside on the eighteenth day of illness, the pulse became gradually weaker, and the patient died on the twenty-second day of illness, purely of cardiac failure. Two days before death the urine was found to contain blood and to present the same colour before noted in cases of pyelitis. In this instance, however, the guaiacum reaction for blood was very marked. The sediment in the urine consisted of red blood cells and tailed epithelial cells, few pus cells being observed, and no tube-casts. On the day of death the characters were similar. The diagnosis of pyelitis was made and verified *post-mortem*.

A general review of the preceding cases shows that the symptoms which have been uniformly present have related solely to the urinary condition; the onset has, in the five cases recorded, developed in one at the end of a primary attack of enteric fever (Case V), in one in the apyretic interval between the end of the primary fever and the beginning of a relapse (Case IV), and in the remaining two shortly after the temperature became normal. In none was it ushered in by any special symptoms such as rigor, alteration of pulse or temperature, or special feeling of discomfort. In all cases the first sign to be noted was the altered colour of the urine, which in place of being amber-coloured was of a red hue, of greater or lesser intensity, such as is associated with the presence of blood. The sediment at this stage consisted largely of altered blood cells and of catarrhal epithelial cells such as are found when the epithelial structures of

the urinary tract are inflamed. This, in two cases, was succeeded on the third day by the presence of epithelial and granular casts, indicating inflammation of the kidney. In both instances where these casts were present there was a very considerable amount of albumen in the urine, much out of proportion to that which the presence of blood would account for. In both these cases it is to be noted that the symptoms of nephritis disappeared in five or six days. The symptoms, then, which remain belonging to pyelitis proper seem to be the presence of blood in the urine, with a certain amount of tailed epithelium, which rapidly, in two or three days, is replaced by the ordinary pus cells and the protracted appearance of the latter in the urine. In two cases the origin of this pus was more or less identified with the pelvis of the kidney by the result of palpation, in Case IV by tenderness in the region of the left kidney; in another (Case I) the absence of pus in the urine for two days was found associated with a definite enlargement of the left kidney which could no longer be perceived after the passing of a specimen of urine largely consisting of pus. One interesting point in connection with the presence of blood in the urine in pyelitis is the difficulty with which the characteristic reaction with guaiacum is frequently obtained. Unfortunately, spectroscopic examinations were not made in any of the cases. The blood always occurs with the onset of the illness, but may continue to appear in small quantities and at irregular intervals for some time after the condition has become established. The light thrown on the clinical symptoms by the pathological description by Dr. Chapman is considerable. The focal lesion in the kidney explains the temporary nephritis observed in two instances as well as the presence of a certain amount of blood in the urine, while the degree of congestion and apparent fragility of the blood-vessels of the pelvis which are subjacent to the epithelial surface is such as cannot but cause marked hæmorrhage, resulting in the pigmentation of the urine referred to.

The duration of the condition is seen to be very variable; in one case the whole course occupied no more than six days, in another it lasted twenty-two days, while in other two pus was still present in the urine in minute quantity about three months after the onset.

Post-mortem appearances in a case of enteric pyelitis, by E. S. Chapman, M.D.—The occurrence of pyelitis as a complication in enteric fever is of some rarity. The literature

upon the subject is scanty, and practically no references have been made to the pathological alterations found in the pyelon. A description, therefore, of the pathological changes found in the pelvis of the kidney in a case of this condition may be of some interest.

The following is an extract from the report made at the autopsy of N. L., who died at Belvidere Hospital on 29th August, 1905, during an attack of enteric fever. During the illness there had been symptoms pointing to the presence of pyelitis. The symptoms have already been fully discussed by Dr. Brownlee.

"The body was that of a well-nourished man. The heart was enveloped in a considerable amount of fatty tissue. The heart muscle showed much albuminoid degeneration. The valvular structures were normal. The pericardium contained a normal amount of serous fluid and showed no signs of inflammation. The bases of both lungs were intensely congested, but no other pulmonary lesion was present. There was no evidence of peritonitis. The liver was fatty, and the gall-bladder was distended and contained a considerable quantity of bile, in which floated numerous flocculæ. The walls of the gall-bladder were congested, but no ulceration was visible. Cultures made by Dr. R. M. Buchanan from the bile showed a pure growth of the bacillus typhosus. The spleen was congested, and a section showed many small hæmorrhages.

"The lower part of the small intestine was much congested and the mucous surface exhibited numerous solitary ulcers. The Peyer's patches situated at some distance from the ileo-cæcal valve were deeply ulcerated, while those in the immediate neighbourhood of the valve showed little of the characteristic foveation, a condition suggestive of healing of the ulcers in the lowest portion of the small bowel. The mesenteric glands were much swollen and congested.

"The left kidney weighed $4\frac{3}{4}$ oz. The capsule was non-adherent. On section it showed a slight degree of fatty degeneration and some congestion of the pyramids. The pyelon was normal, but the ureter appeared to be somewhat larger than normal. The right kidney weighed $3\frac{3}{4}$ oz. The capsule was non-adherent. On section it showed slight fatty change and some congestion both of the cortex and pyramids. Extending up from one pyramid into the boundary zone there was a localised area, measuring half an inch in length by an eighth of an inch in breadth, which was paler than the neighbouring tissue, and which was surrounded by a thin zone

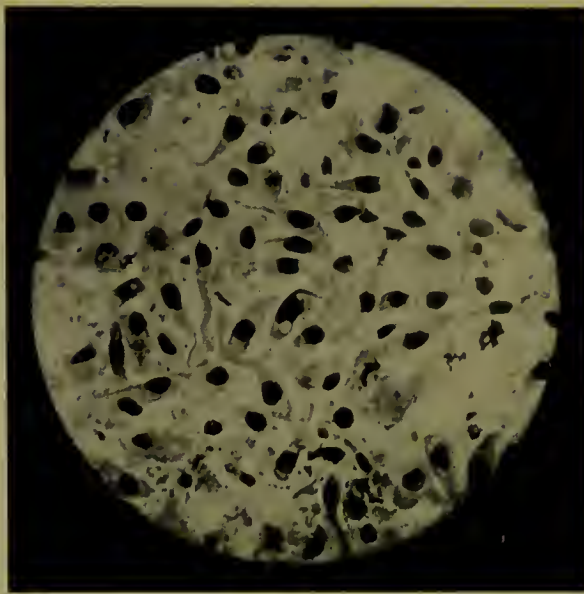


FIG. 1.

Smear preparation of the contents of the pyelon, showing tailed cells and groups of organisms.

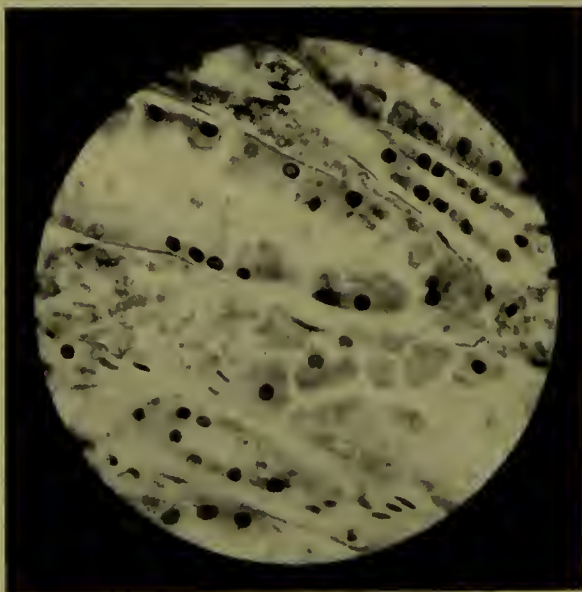


FIG. 2.

Section of kidney showing the presence of large numbers of red blood corpuscles in the epithelial tubules.

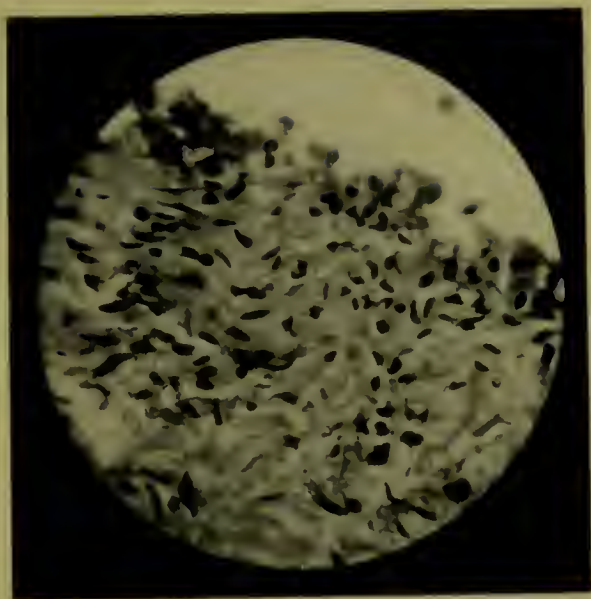


FIG. 3.

Vertical section of the pylon showing catarrhal state of the epithelium.

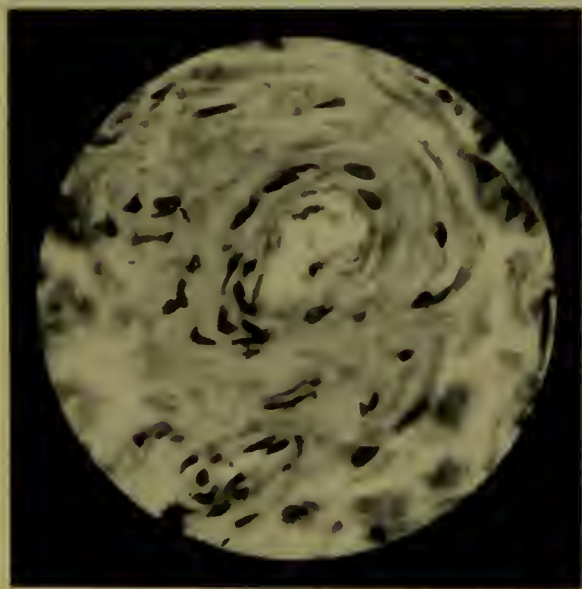


FIG. 4.

Section of an artery in the muscular layer of the pelvis of the kidney, showing thickened walls.

of marked hyperæmia. The pyelon of this kidney was seen to be markedly congested, and the pelvis contained some thin, slightly blood-stained opaque fluid. The fluid was examined bacteriologically by Dr. R. M. Buchanan, and was found to give an almost pure culture of the bacillus typhosus. Microscopically the cells in the fluid consisted almost entirely of the tail-shaped cubical epithelium normally found lining the pelvis together with a few blood corpuscles. Only very rarely were any pus cells seen. The right ureter was of normal size, and did not show any marked congestion. The urinary bladder was normal in appearance, and contained a large quantity of deeply blood-stained urine.

“Portions of the kidney and pyelon tissue were embedded in paraffin after having been fixed and hardened in alcohol, Zenker's fluid, or formaldehyde. The sections were in the majority of instances stained with Ehrlich's acid hæmatoxylin and eosin.

“The chief changes found in the kidney were an extreme degree of congestion, together with some hæmorrhages and degeneration of the tubular epithelium. The intertubular capillaries as well as the larger vessels were seen to be filled with blood cells, and in many places the smaller vessels had ruptured, thus giving rise to small interstitial hæmorrhages, while in some instances the basement membranes of the tubules had been destroyed with consequent hæmorrhage into the tubules. This change was most marked in the localised lesion above referred to, where it was found that the tubular structures were much compressed and partially destroyed by the congestion and hæmorrhages. No evidence of infarction was discovered in this area. The cells in the convoluted tubules exhibited a marked degree of granular degeneration, and in many instances had become separated from the basement membrane. Occasionally there was found necrosis of these cells, and frequently the convoluted tubules were seen to be filled with blood cells and granular *débris*, the latter formed from the disintegration of the tubular epithelium. The cells in the loops of Henle, and those of the functional and collecting tubules also, showed granular degeneration, and in the latter structures hyaline and more rarely granular tube-casts were visible. There was no evidence of any proliferation of the tubular epithelium. The capillaries of the glomeruli were distended with blood cells, and in a few cases there was some hyaline thickening afferent vessels, but apart from these changes there were no gross alterations seen in the Malpighian corpuscles.

“Normally the mucous membrane of the pelvis of the kidney is partly composed of stratified epithelium consisting of four layers. The most superficial cells are cubical in shape. These fit upon the rounded bends of the second layer of cells, which are pear-shaped, and these again are superimposed upon a double layer of tail-shaped epithelium. Beneath this epithelium lining the mucous membrane is composed of areolar tissue which, towards the muscular coat, has loose and open structure. There is, however, no marked distinction between mucous and submucous layers.

“The most marked pathological change found in this pyelon was the destruction of the epithelial cells. The degree of the destruction was not of the same intensity throughout the sections. Over the greater part of the pelvic surface the superficial cells had become separated, only a few of the deeper or tail-shaped cells remaining, while in the remaining areas the degeneration of the epithelium was complete, and the connective tissue of the mucous membrane was found to be directly exposed. In areas showing the partial degeneration some of the remaining tail-shaped epithelial cells were found to have already assumed a somewhat flattened appearance. In a few limited areas there was seen some proliferation of the cells of the deeper layers. These newly-formed cells were tail-shaped and contained one nucleus. No mitotic figures were present. Those situated most superficially were completely separated from the mucous membrane, and were seen, together with many red blood corpuscles, to be lying free upon the surface of the pyelon. All the vessels of the mucous membrane were much congested, and some of the smaller ones had ruptured, thus giving rise to small hæmorrhages. These hæmorrhages were most frequent around the vessels situated immediately below the epithelial covering. In some instances it would appear that these sub-epithelial hæmorrhages were responsible for the degeneration of the epithelium, and occasionally the tissue was so cut as to show the rupture of a vessel situated at the extreme edge of the section, which thus caused a hæmorrhage upon the surface of the pyelon. Rarely was there found any infiltration of the mucous membrane, and when present it was situated in the superficial layers. The infiltrating cells consisted of lymphocytes, and only very occasionally were any polymorphonucleated leucocytes seen.

“The vessels of the muscular layer were congested, and some of the larger ones were thickened. This thickening appeared to be due to an increase in the medial and adventitial coats.

There was no cellular infiltration in this region, and the muscular fibres were found to be normal."

Report by Dr. R. M. Buchanan.—On 30th August Dr. Brownlee submitted cultures from the pylon of the right kidney and from the gall-bladder of N. L., made at the time of *post-mortem* (thirty hours after death). It was stated by Dr. Brownlee that the case presented the characteristic lesions of enteric fever in the ileum, viz., ulceration with healing, suggesting an illness of about five weeks' duration. The pylon of the right kidney was congested in patches, and contained reddish purulent fluid, which on microscopical examination consisted of tailed epithelium, red blood corpuscles, and very few leucocytes. Sparse groups of a bacillus were seen. The gall-bladder was distended, slightly congested, and contained about 4 oz. of fluid showing very numerous flocculi. The bladder appeared quite normal.

The cultures received were growths on sloped agar, the one from the kidney being mixed, the one from the gall-bladder being pure.

An organism showing the characteristic cultural reactions of bacillus typhosus was obtained from each tube, and was confirmed by agglutination tests performed with blood obtained from typhoid cases.

